World Applied Sciences Journal 37 (2): 88-97, 2019
ISSN 1818-4952

DOI: 10.5829/idosi.wasj.2019.88.97

Endophytic Fungi and Their Biological, Biomedical and Biotechnological Applications

[1,2]*Azhar Abdullah Najjar*

[1]Department of Biological Sciences, Faculty of Science,
P.O. Box: 80203, King Abdulaziz University, Jeddah, 21589, Saudi Arabia
[2]King Fahad Medical Research Center,
P.O. Box: 80216, King Abdulaziz University, Jeddah, 21589, Saudi Arabia

Abstract: Endogenous fungi that live in the internal tissues of living plants attract the attention of ecologists, taxonomists, chemists, and agronomists, who have been studied so far. Recent endophytes studies on fungi are exploring the potential use of biomedical drugs. Most studies have shown that these fungi are particularly notable in biotechnology in an impressive range, as biocontrol agents. They said to have qualifying applications; agricultural control, plant growth stimulants, environmental stress reductions and bioremediation are required. In addition, forest mushrooms endophytes may be an underutilized reservoir of new exploited biological resources in the pharmaceutical, industrial and agricultural areas. This review focused on endophytic fungi and their biological, biomedical and biotechnological applications.

Key words: Endophytic · Fungi · Biological · Biomedical · Applications

INTRODUCTION

Endophytes from plants are a vast new resource for research. Most plants are screened for their therapeutic applications of pharmaceutical phytochemical determined and analyzed used different methods. The first technique for selection, extraction solvent of choice is composed of revolutions need biology technique for obtaining the resources to groups considered and bioactive potential biological models [1]. In this technique, organic solvents (methanol, ethanol, acetone, ethyl acetate, chloroform and hexane) and inorganic solvents (water) are used. Between the monthly observations, including the use of ethyl acetate as a fungal endophyte of his studies for extraction with ethyl acetate, removes his revolutions now and pharmaceutical values phenolic compounds. Further, high-through put screening of ethyl acetate to drugs. Marostica endophytes of medicinal plants that are essential to extract a compound without interest harvesting of plants [2]. Therefore, the cultivation skills host mushrooms are the simplest way to produce biologically active compounds in their revolutions only a vast growing competition [3, 4], Studies of endophytic fungi facilitate the detection of biologically active natural compounds and provide better knowledge of secondary metabolites that produce microorganisms with their biosynthesis pathways. Advances in biotechnology leading to identification at the molecular level have led to the development of simple methods and methods for screening fungal isolates from the environment for the sequential extraction of new biologically active compounds. In addition, new techniques facilitate overexpression of individual gene pools and facilitate the use of microorganisms in the industrial field for the large-scale synthesis of biologically important molecules [5].

Fungi found in living plant tissues without visible damage are called endogenous fungi [6]. These fungi mainly live in various organs (roots, stems, leaves, flowers, fruits and seeds) of host plants in the intercellular or intracellular space. Please note that among the approximately 300, 000 plant species on our planet, each plant is considered to contain at least one endogenous fungus. However, only a few of these endogenous plant-

Corresponding Author: Azhar Abdullah Najjar, Department of Biological Sciences, Faculty of Science, P.O. Box: 80203, King Abdulaziz University, Jeddah, 21589, Saudi Arabia., King Fahad Medical Research Center, P.O. Box: 80216, King Abdulaziz University, Jeddah, 21589, Saudi Arabia.

related fungi have been studied, indicating that they can find endogenous plants of interest from different plants from different niches and ecosystems. In addition, studies on endogenous fungi in plants are necessary to assess the diversity and distribution of fungi around the world, as well as to provide basic information for the detection of new species. Until now, Ascomycota, Basidiomycota and Zygomycota are included in the endophytic classification group of various plant species [7]. Recent studies have revealed various metabolites that differ in endogenous species diversity and function in some cases, they promote plant growth, act as biological control agents [8] and can produce enzymes. Endogenous fungi are relatively unexplored and may be potential sources of new natural products for use in medicine, agriculture and industry [9].

The fungi studied on plants seemed to be outstanding symbionts. Endophytes of leaves and shoots are increasingly recognized due to their influence on the health and usefulness of host plants. In addition, since endophytic mushrooms are easily grown, they allow laboratory studies of the ecology of natural systems under controlled conditions. Fungal endophytes are intercellular asymptomatic communities inhabiting various host plants and most of them do not cause disease To the host [10]. We can define endophytic fungi as symbiotes, which mysteriously reside in healthy leaves and shoots and can horizontally be transferred between hosts [11] Several studies have shown that in most cases there is an interaction between a large group of endophytic microorganisms and the hosts with whom they lived , an interaction that can be classified as a common benefit for plants and microorganisms. These useful mushrooms protect their host from harmful agents and facilitate the adaptation of plants in adverse environmental conditions [12, 13]. They attracted considerable attention due to the diverse biological applications in agriculture, industry and medicine since their properties of producing bioactive secondary metabolites are relatively little studied. The purpose of this work was to provide an overview of endophytic fungi and their biological and biomedical applications.

Isolation and Cultivation of Endophytic Fungi: In early 1898, endogenous fungi were isolated for the first time from plant seeds. This indicates that fungi can be closely related to plants. However, from 1890 to 1980, only a few endogenous fungi were recorded [14]. Since the 1980s, endogenous fungi have been isolated from almost all tracheal parasites studied, from grasses to woody plants. Colonization of terrestrial plants by fungi is widespread. Endogenous fungi are therefore an important component. Biodiversity of microorganisms with root plant species. In theory, any plant can be selected to isolate the fungus [15] have shown that plant breeding is tactical. These plants with non-traditional bases and biology and well-established ethnic botanical value will be a promising and preferred source of endogenous fungi to produce new biologically active products. Let's see. Isolation is the most important step to obtain a pure culture and the host species is the sampling strategy, the interaction between the host and the endogenous fungi, the type and age of the tissue, its distribution geographical and habitat growing conditions, surface disinfectant and selective medium affect the detection. And enumeration of endophytic fungi examined several detailed separation methods and procedures, including plant sampling, surface sterilization and media [16]. Plant breeding is important for the isolation of new endogenous fungi, as well as for those producing new biologically active products and selection strategies are described [16].

Surface sterilization is an important first step to avoid contamination of plant surfaces and isolate endophytic fungi. Sodium hypochlorite (2 to 10%), ethanol (70 to 90%), H 2 O 2 (3%), KMnO4 (2%) are generally used as a surface disinfectant. Ethanol sterilization is widely used, followed by sodium hypochlorite [9, 17]. Several surfactants such as Tween 20, Tween 80 and Triton X-100 have been used as absorbents to improve the effectiveness of surface sterilization [15, 18]. Common protocols include a three-step procedure described by Coombs and Franco [18]. The five-step procedure was introduced by Qin *et al*. [15], a solution of sodium thiosulfate is added after treatment with sodium hypochlorite as this sulfate decreases residual traces of NaClO and promotes entophyte growth and release. In general, sensitivity varies with species, organ and age, so surface sterilization procedures should be optimized for each plant tissue, especially for the duration of sterilization [15]. In addition to surface sterilization, vacuum and bomb technologies have been used to isolate endogenous fungi [19].

Biotechnological Applications of Endophytic Fungi

Agricultural Control: Studies have shown that endophytic fungi can confirm pathogen resistance to their host plants through direct secretion of antimicrobial substances. Available evidence suggests that endophytes may enhance protection against congenital

Fig. 1: Endophytic fungal diversity in Panama, https://cals.arizona.edu/spls/news/research/endophytic-fungal-diversity-panama

pathogens and herbivores. Some endophytic studies show that plant-secreted antimicrobials can potentially be used as drugs to treat human diseases and some forms of agricultural control [20].

Plant organs appear to have no pathological symptoms when the host develops endophytes. In fact, improved growth is shown, as well as improved nutrient absorption. We can also detect an improvement in the quality and productivity of economically important crop species by endophytes when introduced into endophytic fungal symbionts [21]. Endophytes can also have a negative impact, although they have not yet been detected here, we are more interested in mentioning the benefits of endophytic mushrooms, especially those associated with improved agriculture or increased crop production. Endophytic fungi, as a rule, can protect plants from pathogenic microorganisms in two ways: a. Development of auxiliary metabolites, such as phytoalexins and b. Improvement of the natural habitat [22]. Endophytes can improve the NUE of a plant through several mechanisms, including the formation of excess root hyphae to absorb nutrients, stimulate root growth and modify plant metabolism, promoting nutrient absorption; nitrogen and phosphate, nitrogen fixation and direct or modified modification of root exudates. Many endogenous strains have been found, but commercially available endogenous inoculants are limited to Rhizobium, Horwich, Aspergillum and arbuscular [23]. Plants provide food for endophytes, while endophytes protect them against pathogenic microorganisms, durability and stress [24]. These infectious proteins play an important role in biodegradation and hydrolysis, an essential element in the fight against contamination by pathogens isolated from the treated plant *Asclepias sinaica*, *Penicillium chrysogenum* Pc -25, *Alternative alternaria* Aa-27, the third infectious strain was identified as the sterile pituitary. The combination of Asco or Basidiomycota endophytes with plant tissue powder can increase the overall tolerance of plants [25]. *Lewia sp.* increase the concentration of plant H2O2 and malonic dialdehyde and reduce the activity and development of glutathione-S-transferase (GST). In addition, *Lewia sp.* reduce the concentration of H2O2 in the progress of HCM plants and increase the movement of superoxide dismutase and peroxidases.

Endophytes also affect agroforestry products and their relationship with plants is to improve plant growth on poor soils and soils, as well as in areas where there is an insufficient amount of fertilizers and pesticides. This means that endophytes must be grown in plants. *P. indica* of the Seminoles order is multiform in their endophytic relationships. This can improve the growth of the host. This endophyte was unknown and was a force universally hidden in plant ecosystems. It colonizes the roots; as a result, nutrient uptake is increased, rapid flowering occurs, seed yield increases and adapts to complex biotic and abiotic factors. Inoculated plants of *P. indica* are resistant to salt and root parasites as shown in Fig. 2 & 3, [4, 13].

Environmental Stress: To reduce stress without compromising plant growth and yield, an ideal strategy has been proposed. A fungal association that promotes plant growth is seen as beneficial to host plants under stress. Fungal endophytes play a vital role in the life cycle of a plant. It has a direct effect on plant growth and nutrient absorption. In recent decades, endophytic fungi have drawn the attention of crop scientists to a possible way to increase plant resistance in a rapidly changing environment, without the effects of toxicity or pathogenicity [28]. Fungi are considered one of the most important plant's growth factors because they play an important role in the transformation of rocks and minerals. And it has been classified as a support to improve the performance of the facilities. All plants have a salt-sensitive metabolism, where they grow in high salt

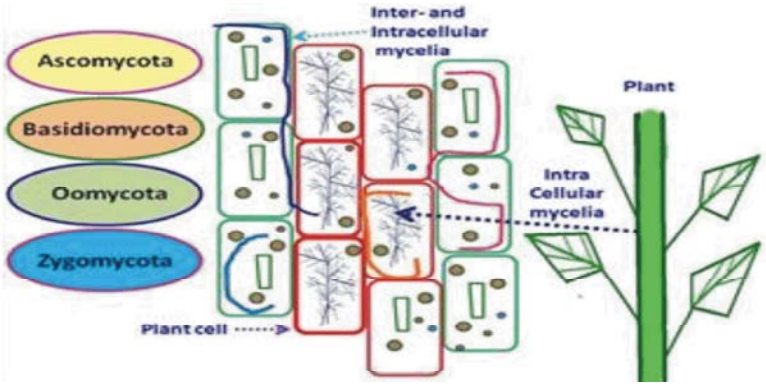

Fig. 2: Classification of endophytic fungi and existence in plant cell [26]

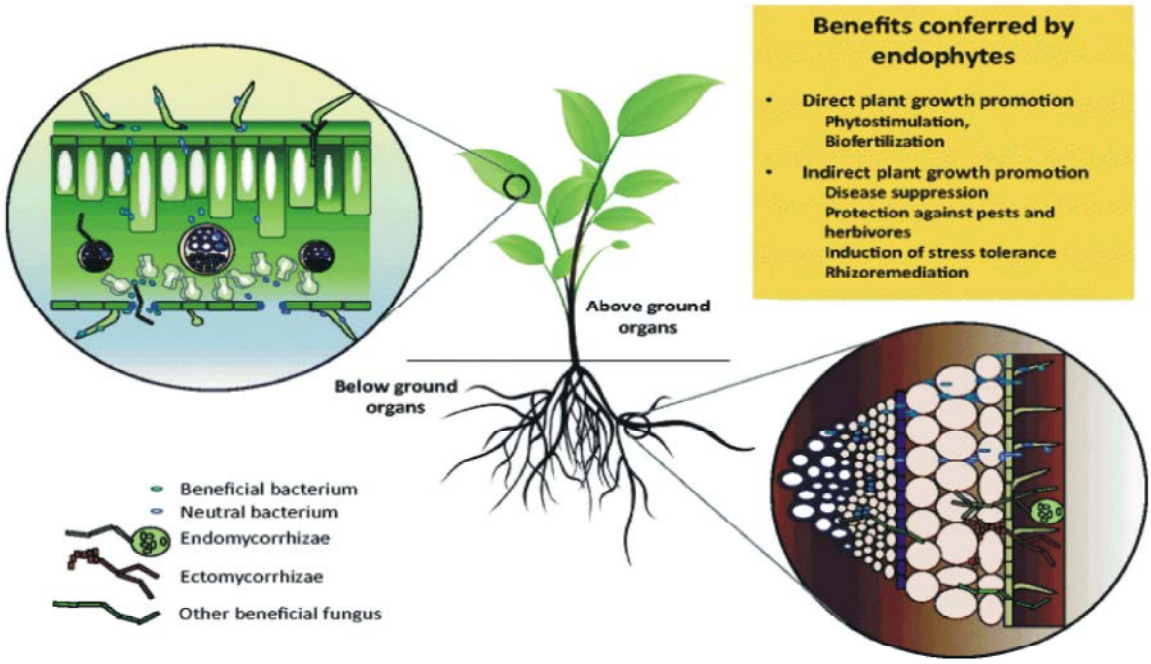

Fig. 3: Drawing showing the niches inside plants and ways of colonization of endophytes [27]

concentrations; such as growth in salt marshes or low salt concentrations; like growth in the temperate rainforest. Some mycorrhizal fungi confirm a symbiosis of salt tolerance [28, 29].

Salinity and drought have been articulated and determined more clearly around the world, posing a significant risk to a managed generation of farmers. Due to global temperature changes, the rate of dispersion in the saline soil changes regularly causing reactive oxygen species (ROS), which form under such extreme conditions in plants and cause death. cells during prolonged exposure [21], Evaluated the symbiotic association of endophytic fungi, *Penicillium sp.* And with the advancement of host plant biomass under saline and drought conditions.

Soil salinization is the main obstacle to plant growth and can alter the osmotic capacity of the soil solution. An earlier study had shown that inoculation with the fungal endophyte reduced salt stress, which negatively affected wild barley [30]. In addition, they are potentially exposed by various hosts to abiotic factors, such as drought and pressure. In previous studies, various strains of fungal endophytes had been exposed to rice to increase soil resistance to drought and revealed the exudation of gibberellins from these beneficial fungi that can improve root formation parameters and plant growth without any side effects [31]. Other researchers have developed a study of an endophytic fungus (Actinomyces sorboses LHL10), which is found at the root of a cucumber plant with a symbiosis secreting

certain phytohormones, such as gibberellins (GA) (GA1, GA3, GA4, GA8, GA9, GA12). These fungal hormones help improve certain metabolic functions during plant growth, minimizing the effects of salt stress on cucumber leaf tissues and reducing water loss, which provides a higher level of protection against environmental changes Antibiotics [32]. Recent studies have shown that fungal endophytes can improve the ecological adaptation of plants living in adverse conditions and increase their resistance to biotic conditions. We need to study the types of endophytes of Saudi fungi, which could be useful for biological control of environmental stress and other applications. Many studies have been discovered that could improve the quality and productivity of economically important crop species due to interactions between endophytic fungi. Bioremediation with other biological roles fungal endophytes, which reduce the toxicity of plants because of heavy metal contamination in the fields. This pollutant is a major problem in sustainable agriculture and industrial areas, considered a source of toxins for plants. The endophyte-metal-plant interaction has been shown to be effective in reducing toxicity levels, which is considered an excellent way to increase the efficiency of crop production. Understanding the resistance of gibberellins producing endophytic fungi to agricultural plants on agricultural soils contaminated with metals may.

Plant Growth Agents: Environmental problems caused by pesticides and chemical fertilizers directly or indirectly prompted researchers to consider alternatives that promote plant growth in agriculture. Endophytic fungi are of interest because they have many properties that promote plant growth. The beneficial effect of plant growth promoting fungi (PGPF) on plant growth and development is well documented [33]. The promising plant growth mechanisms studied include the production of biological regulators, phytohormones (indole acetic acid, gibberellins, cytokines, etc.), Siderophore, which binds Fe3 + in the environment, increasing nutrient absorption by the host and releasing substances (Fig. 4), suppression of ethylene production by 1-aminocyclopropane-1-carboxylate (ACC) deaminase activity [34-36]. For example, *Phumla sp.* Fungal endophyte. GAH7, isolated from cucumber roots, produced large quantities of GA3, GA4, GA9and GA19, which served as controls to produce AGs [34]. Endophytic LHL 10 from cucumber roots can promote plant growth by producing large amounts of IAA and AG [35]. The properties of endophytic fungi that promote plant growth and the recent deepening of our understanding of some of the mechanisms, suggest that this promising source deserves further study for potential use in agricultural production.

The Role of Endophytic Fungi and the Possibility of New Secondary Biologically Active Metabolites: Endogenous fungi have a long-term relationship with host plants and many endogenous fungi produce biologically active compounds [38]. Endophytes: a potential resource for biosynthesis, biotransformation and biodegradation. Therefore, endogenous fungi and host plants have similar methods for synthesizing secondary metabolites by horizontal gene transfer [38, 39] and endogenous fungi have new product It was hypothesized that it could be an important source of secondary biological activity. Metabolite product hasmany biologically active substances such as *cryptocan, gentiopyrine, spiroquinazoline* alkaloid, *taxol,* vinblastine, vincristine, etc. are potentially useful in modern medicine [40, 41]. Several new physiologically active secondary metabolites [42-48] produced by fungal endophytes show clear interest in the next metabolite.

Biological Control Agent: As shown in Fig. 1, the use of endogenous fungi as a biological control agent against plant pathogens has attracted many researchers since this group of fungi shows the ability to form colonies in plants and antifungal activity. They represent opportunities. *Aspergillus fumigatus*, *Botrytis cinerea, Blumeria graminis, Fusarium culmorum, F. oxysporum, Globi sporangiumultimum, Monilinia laxa, Moniliophthora perniciosa, Penicillium expansum,* to protect plants from various soil pathogens, including and Verticillium longisporum [49, 50]. Endogenous fungi and their role as BCA were discussed in part [50]. The reported biocontrol mechanisms include antibiotics, enzymes that destroy cell walls, myco parasitism, induction of defense responses, the competition of nutrients and space [49]. Pseudomycetes, Piriformospora indica of basidiomycetes that form colonies on plant roots can cause the resistance of barley to phytopathogenic *F. culmorum* [51]. Seven endogenous isolates of *Theobroma cacao* and *T. grandiflorum* belonging to the genus *Curvularia, Fusarium, Pestalotiopsis and Tolypocladium* revealed the biological effects on *P. palivora*, a causative agent for black rot. Cocoa disease [13, 52]. Biological control of fungi is an interesting research field that is rapidly developing and affects plant productivity, health, food security and the environment. Endogenous fungi should be a potential source of ACA development as shown in Fig. 5.

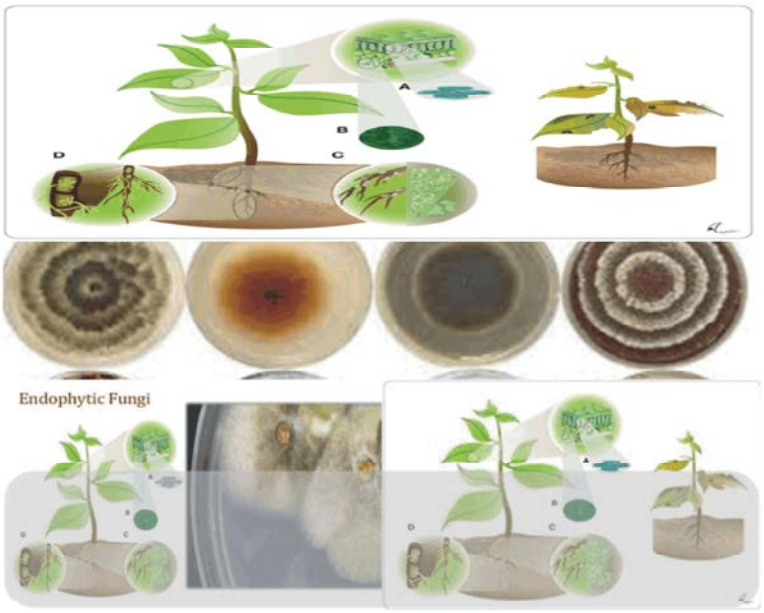

Fig. 4: Microbial Ecology: Endophytes fungi-improved growth traditional plant [37]

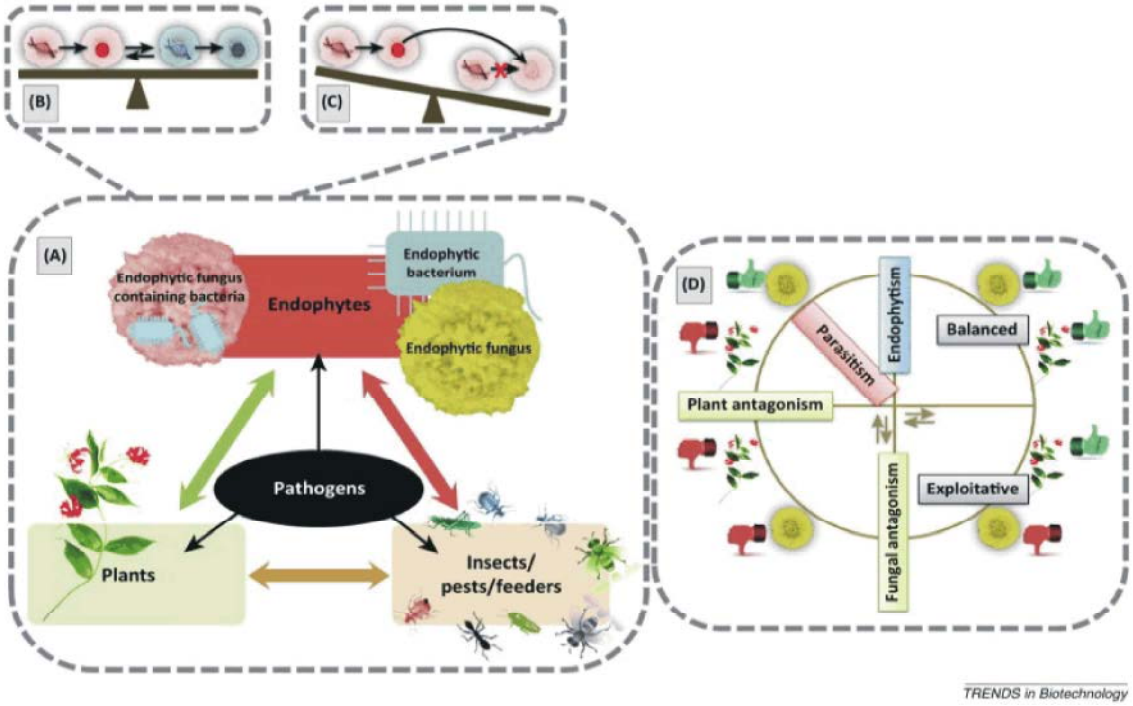

Fig. 5: Biotechnological applications of plant-associated endophytic [53]

Current Problems with Endogenous Fungi from Biological Exploration: Biological exploration endophytes capable of producing the desired biologically active secondary metabolites have traditionally been used to identify various "isolated" endophytes isolated from a single host plant to identify "eligible" endophytes with the desired properties including screening. [1]. Endophytes with the classic approach, only a few final fights may be desirable or nonexistent. Other so-called "incompetent" endophytes are rejected without further investigation, resulting in the loss of the full range of natural products they can produce under appropriate conditions and mimic their natural habitat. However, modern genome sequencing strategies have shown that

the number of genes encoding various fungal and fungal biosynthetic enzymes is significantly higher than the known secondary metabolites of these microorganisms [1]. Thus, only a small part of their actual biosynthetic capacity is used, since rejected endophytes can only express part of their biosynthetic genes under standard laboratory conditions in vitro. It is extremely important. As a result, a huge reservoir of "mysterious" natural metabolites has not been used yet. It is even possible for them to produce the desired target compounds in amounts below the detection limit, which is sometimes associated with an important "metabolic background" and different culture conditions. It is, therefore, necessary to understand the chemical and ecological interactions of endophytes to take full advantage of their inexhaustible possibilities of biosynthesis of natural products.

Future Review of Endogenous Biological Exploration of Fungi: Since the interaction of endogenous fungi with host plants and other endogenous fungi requires significant resources, even small changes in the values of *in vitro* culture conditions can affect the type and extent of secondary metabolites that they produce. It is possible that this affects. It is well known that the metabolic processes of microorganisms depend mainly on culture parameters (environment, temperature, pH, salt concentration and incubation time) [1] In addition, co-culture systems can be complemented by a new, innovative biotechnology platform. Evolution, comparison and co-genomics, proteomics, metabolomics, transcriptome, next-generation sequencing technology (NGS) and bioinformatics [3]. This allows you to understand the endophyte system. Activation/ inactivation of the necessary gene cascade leading to intermolecular signal interaction and transduction, gene expression between species and production of the desired compound [1, 4, 47 , 53].

CONCLUSIONS

In the past decade, endogenous fungi have become a topic of research. Further information on the application of endophyte biodiversity, natural products and biotechnology is included in a wide range of publications and should be analyzed regularly for interested readers. Endogenous fungi have abundant biodiversity and are useful in the pharmaceutical, agricultural and industrial fields. Nevertheless, there is only research on endogenous fungi in the beginning.

Remarks and Future Perspectives: In the future, it may be possible to explore and use fungal endoparasites resources in different ways. First, we can find new endogenous fungi from plants under extreme conditions. Second, we should find an appropriate and effective way to find more effective biologically active compounds from many endogenous fungi. Finally, the use of genetic engineering and metabolic regulation to increase the active substance content of known strains would be promising for large-scale production. Further development of important molecular and proteomic technologies for endophytes will help to understand the interactions between plants and endophytes and complex mechanisms. Biological control of plant diseases, bioremediation and the application of biotechnology in the areas of environmental safety and food security should be further considered. The end fight is a human resource and requires close cooperation between interdisciplinary researchers. From the history of human being indicates the medicinal plants are traditional medicine to heal human from injuries and infections. Current research finds the endophytic fungi are an alternative potential resource to produce the desired compounds at in a short time in large quantities at the Lab. Hence endophytic fungi will be a potential resource to biomedical applications.

Conflict of Interest: The authors declare no conflicts of interest.

ACKNOWLEDGMENT

The authors support from the Dept. of Biological Sciences, Faculty of Science, King Abdulaziz University (KAU), Jeddah, KSA.

REFERENCES

1. Scherlach, K. and C. Hertweck, 2009. Triggering cryptic natural product biosynthesis in microorganisms. Org. Biomol. Chem., 7: 1753-1760.
2. Winter, J.M., S. Behnken and C. Hertweck, 2011. The genomicsinspired discovery of natural products. Curr. Opin. Chem. Biol., 15: 22-31.
3. Greenbaum, D., N.M. Luscombe, R. Jansen, J. Qian and M. Gerstein, 2001. Interrelating different types of genomic data, from proteome to secretome: 'coming in on function. Genome Res., 11: 1463-1468.

4. Gopi, K. and M. Jayaprakashvel, 2017. Endophytic Fungi as Novel Bioresource for Biomedical Applications, Research J. Pharm. and Tech., 10(11): 4114-4115
5. Paramanantham, P., S. Pattnaik and B. Siddhardha, 2019. Natural Products from Endophytic Fungi: Synthesis and Applications, Chapter, 5: 83-103. B.P. Singh (ed.), Advances in Endophytic Fungal Research, Fungal Biology, Springer Nature Switzerland AG _ch., 5: 83-103.
6. Wang, Y. and C.C. Dai, 2011. Endophytes: a potential resource for biosynthesis, biotransformation and biodegradation. Ann. Microbiol., 61(2): 207-215.
7. Carvalho, C.R., V.N. Gonçalves, C.B. Pereira, S. Johann, I.V. Galliza, T.M.A. Alves, A. Rabello, M.E.G. Sobral, C.L. Zani, C.A. Rosa and L.H. Rosa, 2012. The diversity, antimicrobial and anticancer activity of endophyticfungi associated with the medicinal plant Stryphnod endronadstringens (Mart.) Coville (Fabaceae) from the Brazilian savannah. Symbiosis, 57(2): 95-107.
8. Zhang, W., L. Xu, L. Yang, Y. Huang, S. Li and Y. Shen , 2014c. Phomopsidone A, a novel depsidone metabolite from the mangrove endophyticfungus Phomopsis sp. A123. Fitoterapia, 96: 146-151.
9. Zheng, Y., Xin-Guo Qiao., Cui-Ping Miao., Kai Liu., You-Wei Chen Li-Hua Xu and Li-Xing Zhao 2016. Diversity, distribution and biotechnological potentialof endophytic fungi, Ann. Microbiol., 66: 529-542.
10. O'Hanlon, K.A., K. Knorr, L.N. Jørgensen, M. Nicolaisen and B. Boelt, 2012. Exploring the potential of symbiotic fungal endophytes in cerealdisease suppression, Biological Control, 63(2): 69-78.
11. Rodriguez, R.J., J.F. White Jr, A.E. Arnold and R.S. Redman, 2009. Fungal endophytes: diversity and functional roles. New Phytol., 182: 314-330.
12. Khan, A.M., T.A. Ponzio, G. Sanchez-Watts, B.G. Stanley, G.I. Hatton and A.G. Watts, 2007. Catecholaminergic Control of Mitogen-Activated Protein Kinase Signaling in paraventricular Neuroendocrine Neurons *In vivo* and *In vitro*: A Proposed Role during Glycemic Challenges, Journal of the Society for Neuroscience, 27(27): 7344-7360.
13. Bramhachari, P.V., S. Anju, G.M. Sheela, T.R. Komaraiah, D. Venkataiah and A.M.V.N. Prathyusha 2019. Secondary, Metabolites from Marine Endophytic Fungi: Emphasis on Recent Advances in Natural Product Research, Ed., Singh, B. P. Advances in Endophytic Fungal Research, Fungal Biology, Springer Nature Switzerland AG 1, Ch., 15: 339-350.
14. Hyde, K.D. and K. Soytong, 2008. The fungal endophyte dilemma. Fungal Divers, 33: 163-173.
15. Qin, S., K. Xing, J.H. Jiang, L.H. Xu and W.J. Li, 2011. Biodiversity, bioactive natural products, and biotechnological potential of plant-associated endophytic actinobacteria. Appl. Microbiol. Biotechnol., 89(3): 457-473.
16. Strobel, G. and B. Daisy, 2003. Bioprospecting for microbial endophytes and their natural products. Microbiol. Mol. Biol. Rev., 67(4): 491-502.
17. Xiong, Z.Q., Y.Y. Yang and N. Zhao, 2013. Diversity of endophytic fungi and screening of fungal paclitaxel producer from Anglojap yew, Taxus media. BMC Microbiol., 13(1): 71.
18. Zhang, H.W., Y.C. Song and R.X. Tan, 2006. Biology and chemistry of endophytes. Nat Prod Rep., 23(5): 753-771.
19. Coombs, J.T. and C.M.M. Franco, 2003. Isolation and identification of actinobacteria from surface-sterilized wheat roots. Appl. Environ. Microbiol., 69(9): 5603-5608.
20. Christian, N., B.K. Whitaker and K. Clay, 2015. Microbiomes: unifying animal and plant systems through the lens of community ecology theory. Frontiers in Microbiology, 6: 869.
21. Waqas, M., A.L. Khan, M. Kamran, M. Hamayun, S.M. Kang, K.Y.H. Im and I.J. Lee, 2012. Endophytic fungi produce gibberellins and indoleacetic acid and promote host-plant growth during stress. Molecules, 17(9): 10754-10773.
22. Gao, Dai and Liu, 2010. 'Mechanisms of fungal endophytes in plant protection against pathogens', 4(13): 1346-1351.
23. Johnston-Monje, D. and M.N. Raizada, 2011. 4.58-Plant and Endophyte relationships: nutrient management. Comprehensive Biotechnology, 2nd edn. Academic, Burlington, pp: 713-727.
24. Martinez-Klimova, E., K. Rodriguez-Pena and S. Sánchez, 2017. Endophytes as sources of antibiotics. Biochemical Pharmacology, 134: 1-17.
25. Hubbard, R.M., C.C. Rhoades, K. Elder and J. Negron, 2013. Changes in transpiration and foliage growth in lodgepole pine trees following mountain pine beetle attack and mechanical girdling. Forest Ecology and Management, 289: 312-317.

26. Rajamanikyam, M., V. Vadlapudi, R. Amanchy and S. M. Upadhyayula, 2017. Endophytic Fungi as Novel Resources of natural Therapeutics, Biological and Applied Sciences, 60: e17160542.
27. Company, S., Kari Saikkonen, Birgit Mitter andrea Campisano and Jesús Mercado-Blanco, 2016. Editorial special issue: soil, plants and endophytes, Plant Soil, 405: 1-11.
28. Hyungmin, R., H. Marian, L.K. Shyam, C. Johanna, L.D. Sharon and K. Soo-Hyung, 2018. Do Endophytes Promote Growth of Host Plants Under Stress? A Meta-Analysis on Plant Stress Mitigation by Endophytes. Microbial Ecology, 75(2): 407-18.
29. Al-Karaki, G.N., R. Hammad and M. Rusan, 2001. The response of two tomato cultivars differing in salt tolerance to inoculation with mycorrhizal fungi under salt stress. Mycorrhiza, 11: 43-47.
30. Yano-Melo, A.M., O.J. Saggin and L.C. Maia, 2003. Tolarence of mycorrhized banana (Musa sp. cv. Pacovan) plantlet to salin stress. Agric Ecosyst Environ., 95: 343-348.
31. Taixiang, C., J. Richard, C. Shuihong, L.V. Hui, Z. Jingle and L. Chunjie, 2018. “Infection by the Fungal Endophyte EpichloëBromicola Enhances the Tolerance of Wild Barley (Hordeumbrevisubulatum) to Salt and Alkali Stresses.” Plant and Soil, 428(1-2): 353-70.
32. Arvid, H., 2017. Effects of a fungal endophyte on drought tolerance in rice, MSC Thesis (Put type of thesis, Faculty and University, pp: 1-35.
33. Khan, A., Muhammad Hamayun, Sang-Mo Kang, Yoon-Ha Kim, Hee-Young Jung and Joong-Hwan Lee, 2013. Endophytic fungal association via gibberellins and indole acetic acid can improve plant growth under abiotic stress: an example of Paecilomycesformosus LHL10xKhan *et al*. BMC Microbiology, 12: 3.
34. Hamayun, M., S.A. Khan, A.L. Khan, D.S. Tang, J. Hussain, B. Ahmad, Y. Anwar and I.J. Lee, 2010. Growth promotion of cucumber by pure cultures of gibberellin-producing Phoma sp. GAH7. World J. Microbiol. Biotechnol., 26(5): 889-894.
35. Khan, A.L., M. Hamayun, S.M. Kang, Y.H. Kim, H.Y. Jung, J.H. Lee and I.J. Lee, 2012a. Endophytic fungal association via gibberellins and indoleacetic acid can improve plant growth under abiotic stress: an example of Paecilomycesformosus LHL10. BMC Microbiol., 12(1): 3.
36. Khan, A.L., M. Hamayun, S.A. Khan, S.M. Kang, Z.K. Shinwari, M. Kamran, S. Rehman, J.G. Kim and I.J. Lee, 2012b. Pure culture of Metarhiziumanisopliae LHL07 reprograms soybean to higher growth and mitigates salt stress. World J. Microbiol. Biotechnol., 28(4): 1483-1494.
37. Wijesooriya, W.A.D.K. and N. Deshappriya, 2016. An inoculum of endophytic fungi for improved growth of a traditional rice variety in Sri Lanka, tropical Plant Research, 3(3): 470-480.
38. Khan, A.L. and I.J. Lee, 2013. Endophytic Penicillium funiculosum LHL06secretes gibberellin that reprograms *Glycine max* L. growth durin gcopper stress. BMC Plant Biol., 13(1): 86.
39. Wang, Y. and C.C. Dai, 2011. Endophytes: a potential resource for biosynthesis, biotransformation and biodegradation. Ann. Microbiol., 61(2): 207-215.
40. Soliman, S.S.M., C.P. Trobacher, R. Tsao, J.S. Greenwood and M.N. Raizada, 2013. A fungal endophyte induces transcription of genes encodinga redundant fungicide pathway in its host plant. BMC Plant Biol., 13(1): 93.
41. Kumar, S. and N. Kaushik, 2013. Endophytic fungi isolated from oil-seed cropJatropha curcas produces oil and exhibits antifungal activity. PLoSOne, 8(2): e56202.
42. Xiao, J., Q. Zhang, Y.Q. Gao, J.J. Tang, A.L. Zhang and J.M. Gao, 2014. Secondary metabolites from the endophytic Botryosphaeriadothidea of Meliaazedarach and their antifungal, antibacterial, antioxidant and cytotoxic activities. J. Agric. Food Chem., 62: 3584-3590.
43. Zhang, D., H. Ge, J. Zou, X. Tao, R. Chen and J. Dai, 2014a. Periconianone A, anew 6/6/6 carbocyclic sesquiterpenoid from the endophytic fungus Periconia sp. with neural anti-inflammatory activity. Org Lett., 16(5): 1410-1413.
44. Zhang, Q.H., J. Zhang, L. Yang, L. Zhang, D.H. Jiang, W.D. Chen and G.Q. Li, 2014b. Diversity and biocontrol potential of endophytic fungi in Brassica napus. Biol Control, 72: 98-108.
45. Zhou, X.M., C.J. Zheng, G.Y. Chen, X.P. Song, C.R. Han, G.N. Li, Y.H. Fu, W.H. Chen and Z.G. Niu, 2014a. Bioactive anthraquinone derivatives from themangrove-derived fungus *Stemphylium* sp. 33231. J. Nat. Prod., 77(9): 2021-2028.

46. Zhou, Z.F., T. Kurtán, X.H. Yang, A. Mándi, M.Y. Geng, B.P. Ye, O. Taglialatela Scafati and Y.W. Guo, 2014b. Penibruguieramine A, a novel pyrrolizidine alkaloid from the endophytic fungus Penicillium sp. GD6 associated with Chinese mangrove Bruguieragymnorrhiza. Org. Lett., 16(5): 1390-1393.
47. Meena, H., S. Hnamte and B. Siddhartha, 2019. Secondary Metabolites from Endophytic Fungi: Chemical Diversity and Application Springer B.P. Singh (ed.), Advances inEndophytic Fungal Research, Fungal Biology, Nature Switzerland AG 2019 145, https://doi.org/10.1007/978-3-030-03589-1_7
48. Hanada, R.E., A.W.V. Pomella, H.S. Costa, J.L. Bezerra, L.L. Loguercio and J.O. Pereira, 2010. Endophytic fungal diversity in Theobroma cacao (cacao) and T. grandiflorum (cupuaçu) trees and their potential for growthpromotion and biocontrol of black-pod disease. Fungal Biol., 114(11): 901-910.
49. Zhang, W., L. Xu, L. Yang, Y. Huang, S. Li and Y. Shen, 2014c. PhomopsidoneA, a novel depsidone metabolite from the mangrove endophyticfungus *Phomopsis* sp. A123. Fitoterapia, 96: 146-151.
50. Backman, P. A. and R.A. Sikora, 2008. Endophytes: an emerging tool for biological control. Biol. Control, 46(1): 1-3.
51. Waller, F., B. Achatz, H. Baltruschat, J. Fodor, K. Becker, M. Fischer, T. Heier, R. Hückelhoven, C. Neumann, D. Von Wettstein, P. Franken and K.H. Kogel, 2005. The endophytic fungus Piriform osporaindica reprograms barley to salt-stress tolerance, disease resistance and higher yield. Proc Natl Acad Sci. USA, 102(38): 13386-13391.
52. Meena, H., S. Hnamte and B. Siddhardha, 2019. Secondary Metabolites from Endophytic Fungi: Chemical Diversity and Application, Springer NatureSwitzerland AG 2019 145 B.P. Singh (ed.), Advances in Endophytic Fungal Research, Fungal Biology, https://doi.org/10.1007/978-3-030-03589-1_7
53. Kusari, S.S. and S. Jayabaskaran, 2014. Biotechnological potential of plant-associated endophytic fungi: hope versus hype trends Biotechnology, 32(6): 297-303.